GP 1743

*PATENT*
Attorney Docket No. **UM-04228**

SAH #6
10-6-00



**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of: Kalyan Handique *et al.*
Serial No.: 09/518,895
Filed: 03/06/00
Entitled: **Moving Microdroplets**

Group No.: 1743
Examiner: J. Warden

# INFORMATION DISCLOSURE STATEMENT TRANSMITTAL

Assistant Commissioner for Patents
Washington, D.C. 20231

**CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8(a)(1)(i)(A)**

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being deposited with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

Dated: October 5, 2000 By: Christopher J. Collins

Sir or Madam:

Enclosed please find an Information Disclosure Statement and Form PTO-1449, including copies of the references contained thereon, for filing in the U.S. Patent and Trademark Office.

This Information Disclosure Statement is being filed under rules set forth in 37 C.F.R. § 1.97(b) (3).

The Commissioner is hereby authorized to charge any additional fee or credit overpayment to our Deposit Account No. **08-1290**. **An originally executed duplicate of this transmittal is enclosed for this purpose.**

Dated: October 5, 2000

Peter G. Carroll
Registration No. 32,837

MEDLEN & CARROLL, LLP
220 Montgomery Street, Suite 2200
San Francisco, California 94104
617/252-3353

*PATENT*
Attorney Docket No. **UM-04228**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of: Kalyan Handique *et al.*
Serial No.: 09/518,895
Filed: 03/06/00
Entitled: **Moving Microdroplets**

Group No.: 1743
Examiner:



# INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

**CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8(a)(1)(i)(A)**

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being deposited with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

Dated: October 5, 2000 By: Christopher J. Collins

Sir or Madam:

The citations listed below, copies attached, may be material to the examination of the above-identified application, and are therefore submitted in compliance with the duty of disclosure defined in 37 C.F.R. §§ 1.56 and 1.97. The Examiner is requested to make these citations of official record in this application.

The following printed publications are referred to in the body of the specification:

- U.S. Patent No. 4,683,195 to Mullis *et al.*;
- U.S. Patent No. 4,683,202 to Mullis *et al.*;
- U.S. Patent No. 4,967,950 to Legg *et al.*;
- U.S. Patent No. 5,091,328 to Miller;
- Marmur and Lane, "Strand Separation and Specific Recombination in Deoxyribonucleic Acids: Biological Studies", *Proc.Nat.Acad.Sci. U.S.A.* 46:453-461 (1960);

- Doty *et al.*,"Strand Separation and Specific Recombination in Deoxyribonucleic Acids:Physical Chemical Studies", *Proc.Nat.Acad.Sci., U.S.A.* 46, 461-477 (1960);
- Hayashi *et al.*,"Restriction of in Vivo Genetic Transcription to one of the Complementary Strands of DNA", *Proc.Nat.Acad.Sci., U.S.A.* 50, 664-671 (1963);
- Smith and Wilcox, "A Restriction Enzyme from *Hemophilus influenzae", J.Mol.Biol.* 51, 379-391 (1970);
- Southern, "Detection of Specific Sequences Among DNA Fragments Separated by Gel Electrophoresis", *J.Mol.Biol.* 98, 503-517 (1975);
- Maxam and Gilbert, "A new method for sequencing DNA", *Proc. Natl. Acad Sci. USA* 74:560-564 (1977);
- Sanger *et al.*, "DNA sequencing with chain-terminating inhibitors", *Proc. Natl. Acad Sci. USA* 74:5463-5467 (1977);
- Sambrook, J. *et al.*, Molecular Cloning, A Laboratory Manual, 2d Ed. Cold Spring Harbor Laboratory Press, New York, 13.7-13.9 (1989);
- Hunkapiller, M.W., "Advances in DNA sequencing technology", *Curr. Op. Gen. Devl.* 1:88-92 (1991);
- Tabor *et al.*, "DNA sequence analysis with a modified bacteriophage T7 DNA polymerase", *Proc. Natl. Acad. Sci. USA* 84:4767-4771 (1987);
- Innis *et al.*, "DNA sequencing with *Thermus aquaticus* DNA polymerase and direct sequencing of polymerase chain reaction-amplified DNA", *Proc. Natl. Acad. Sci. USA* 85:9436-9440 (1988);
- J. Pfahler *et al.*,"Liquid Transport in Micron and Submicron Channels", *Sensors and Actuators,* A21-A23, pp. 431-434 (1990); and
- H.T.G. Van Lintel *et al.*, "A Piezoelectric Micropump Based on Micromachining of Silicon", *Sensors and Actuators* 15:153-167 (1988).

Applicants have become aware of the following printed publications which may be material to the examination of this application:

- Smits, "Piezoelectric Micropump with Three Valves Working Peristaltically," *Sensors and Actuators* A21-A23:203-206 (1990) describe a silicon micropump that can be used to pump liquids or gases to a higher pressure, which can then be relieved through a check valve. The device is intended for use in constant rate delivery of drugs for pain relief or diabetes, cryogenic coolant pumps, etc. The channels are described as hydrophobic. There is no discussion of channels designed for the transport of microdroplets.
- Mullis and Faloona, "Specific Synthesis of DNA *in Vitro* via a Polymerase-Catalyzed Chain Reaction," *Meth. Enzym.* 155:335-350 (1987) describe a method for the synthesis of DNA utilizing a template, primer and DNA polymerase. There is no discussion of a device having microdroplet transport channels with one or more hydrophobic regions.
- Arnheim and Erlich, "Polymerase Chain Reaction Strategy," *Annu. Rev. Biochem.* 61:131-156 (1992) describe methods and strategies for utilizing the Polymerase Chain Reaction. There is no discussion of a device having microdroplet transport channels with one or more hydrophobic regions.
- Nickerson *et al.*, "Automated DNA diagnostics using an ELISA-based oligonucleotide ligation assay," *Proc. Nat. Acad. Sci. USA* 87:8923-8927 (1990) describe a method of DNA diagnostics using amplification of target DNA segments by PCR and discrimination of allelic sequence variants by a colorimetric oligonucleotide ligation assay. There is no discussion of a device having etched microdroplet transport channels with one or more hydrophobic regions.
- Gordon *et al.*, "Capillary Electrophoresis," *Science* 27:224-228 (1988) describe a method of separation of molecules in solution in a capillary tube, including wall coatings and particular solutes in the separation medium to enhance separation and prevent adherence to the capillary walls. There is no discussion of a device having etched microdroplet transport channels with one or more hydrophobic regions.

- Lawrence Berkeley Lab Presentation, Park City, Utah (1993) describes a micro-PCR device. There is no discussion of a device having etched microdroplet transport channels with one or more hydrophobic regions.
- Turner, "New Dimensions in Capillary Electrophoresis Columns," *LC-GC* vol .9 (1991) describes various methods of capillary electrophoresis, including rectangular tubing, wall-coated capillary columns and capillary gel electrophoresis. There is no discussion of a device having etched microdroplet transport channels with one or more hydrophobic regions.
- Heller and Tullis, "Microelectrophoresis for the separation of DNA fragments," *Electrophoresis* 13:512-520 (1992) describe separation of DNA fragments and oligonucleotides in microscopic bands in either capillary tube or thin-layer microgel formats of one centimeter or less in length. Bands are detected using high-resolution electronic imaging systems. There is no discussion of a device having etched microdroplet transport channels with one or more hydrophobic regions.
- Manz *et al.*, "Planar chips technology for miniaturization and integration of separation techniques into monitoring systems Capillary electrophoresis on a chip," *J. Chrom.* 593:253-258 (1992) describe miniaturization of capillary electrophoresis in etched channels on a glass or silicon microchip. There is no discussion of one or more hydrophobic regions in the etched channels.
- Jorgenson and Lukacs, "High-Resolution Separations Based on Electrophoresis and Electroosmosis," *J. Chrom.* 218:209-216 (1981) describe capillary electrophoresis in a 75 micrometer glass capillary and reverse phase chromatography in essentially the same apparatus filled with a packing material. There is no discussion of device having etched microdroplet transport channels with one or more hydrophobic regions.
- Ansorge *et al.*, "High-throughput automated DNA sequencing facility with fluorescent labels at the European Molecular Biology Laboratory," *Electrophoresis* 13:616-619 (1992) describe a facility for automated on-line DNA sequencing for maximum throughput of gel sequencing technology. Improvements leading to increased sequencing output are discussed, including

the use of ultrathin gels with increased separation distance and specific fluorescent labels. There is no discussion of a device having etched microdroplet transport channels with one or more hydrophobic regions.

- Pentoney *et al.*, "A single-fluor approach to DNA sequence determination using high performance capillary electrophoresis," *Electrophoresis* 13:467-474 (1992) describe the use of laser induced fluorescence detection for enzymatic chain termination sequencing of DNA using high performance capillary gel electrophoresis. There is no discussion of a device having etched microdroplet transport channels with one or more hydrophobic regions.
- Daniel *et al.*, French patent #2,672,301 (7-8-92), describe a device to carry out a series of steps to complete a diagnostic test based on molecular hybridization. There is no discussion of the nature of the substrate used for the device, the utilization of etching to create microdroplet transport channels, or the presence of hydrophobic regions within microdroplet transport channels.
- Tenan *et al.*, "Friction in Capillary Systems," *Journal of Applied Physics* 53:6687-6692 (1982), describe and test a model of capillary friction as being related to equilibrium contact angle and "frictional angle", which is a characteristic of the solid surface. There is no discussion of a device having etched microdroplet transport channels with one or more hydrophobic regions.
- Dussan, "On the Spreading of Liquids on Solid Surfaces Static and Dynamic Contact Lines," *Annual Review of Fluid Mechanics* 11:371-400 (1979) describes equations and experimental strategies used to model and investigate static and dynamic contact lines and contact angles. There is no discussion of a device having etched microdroplet transport channels with one or more hydrophobic regions.
- Probstein, "Physicochemical Hydrodynamics," sections 4.3 and 9.5 (1989), describes both channel flow and how spatial gradients in surface tension at a liquid-gas interface can give rise to underlying bulk fluid movement. There is also discussion of how surfactants can affect the pressure drop necessary to push a bubble through a fine capillary. There is no discussion of a device

having etched microdroplet transport channels with one or more hydrophobic regions.

- R.F. Service, "The Incredible Shrinking Laboratory," *Science* 268:26-27 (1995), presents a brief discussion of the impact of microchips on the future of laboratory research. There is no disclosure of a device with a microdroplet transport channel having one or more hydrophobic regions.
- Presentation at Cold Spring Harbor, University of Michigan, Ann Arbor, MI (August 31-September 2, 1995) describes a micro-PCR device on a silicon chip. There is no disclosure of a microdroplet transport channel having one or more hydrophobic regions.
- R. Nowak, "Xeroxing DNA Analysis," describes a silicon chip used to detect specific DNA sequences and briefly discusses the associated hurdles of liquid movement in channels. There is no disclosure of a device with a microdroplet transport channel having one or more hydrophobic regions.
- Z. Liang *et al.*, "Microfabrication of a Planar Absorbance and Fluorescence Cell for Integrated Capillary Electrophoresis Devices," *Anal. Chem.* 68:1040-1046 (1996), describe a glass microchip with etched flow channels and optical detection features (a U-cell and optical fibers) for capillary electrophoresis; Samples are injected as "plugs", using electric fields applied for a certain length of time. There is no disclosure of a microdroplet transport channel having one or more hydrophobic regions.
- Manz, A. *et al.*, "Electroosmotic pumping and electrophoretic separations for miniaturized chemical analysis systems" *J. Micromech. Microeng.* 4:257-265 (1994). This article describes the electrokinetic movement of fluids and solutes within capillary channels on a microfabricated device. There is no discussion of a microdroplet transport channel with one or more hydrophobic regions.
- Wooley and Mathies, "Ultra-High-Speed DNA Sequencing Using Capillary Electrophoresis Chips," *Anal. Chem.* 67:3676-3680 (1995), describes microfabricated capillary electrophoresis chips, which separate sample "plugs" in derivatized and polyacrylamide-filled channels. There is no disclosure of a microdroplet transport channel having one or more hydrophobic regions.

- Effenhauser *et al.*, "Manipulation of Sample Fractions on a Capillary Electrophoresis Chip," *Anal. Chem.* 67:2284-2287 (1995), this reference describes a microfabricated capillary electrophoresis chip with separation of the sample "plug" in gel-filled channels. There is no discussion of a microdroplet transport channel having one or more hydrophobic regions.
- Van der Moolen, J.N. *et al.*, "A Micromachined Injection Device for CZE: Application to Correlation CZE" *Anal. Chem.*, 69:4220-4225 (1997). Van der Moolen, J.N. *et al.* describe a micromachined injection device which may be connected to a capillary. There is no discussion of a device having microdroplet channels with one or more hydrophobic regions.
- P.B. Hieptas *et al.*, "Ultrathin Slab Gel Separations of DNA Using Single Capillary Sample Introduction System," *Anal. Chem.* 69:2292-2298 (1997). The authors disclose electrokinetic sample introduction from a transfer capillary into ultrathin slab gels. The samples are in the form of dsDNA plugs which can be electrophoretically separated on the ultrathin slab gel. There is no discussion of a device with microdroplet transport channels having one or more hydrophobic regions.
- U.S. Patent 5,660,993 to Cathey *et al.* discloses a disposable diagnostic assay device. The device is designed to transport fluid samples through a series of channels, such channels having hydrophilic and hydrophobic regions. There is no disclosure of channels designed to transport microdroplets.
- U.S. Patent 3,799,742 to Coleman discloses a miniaturized analytical test container, through which a liquid or semi-solid sample can pass through various chambers through conduits. The patent mentions introduction of fluid along a wall made hydrophilic near the point of entry but left hydrophobic below this point, so fluid will initially wet only the hydrophilic portion of the wall (column 23, lines 56-75). There is no mention of etched microdroplet transport channels.
- U.S. Patent 5,494,639 to Grzegorzewski discloses a biosensor to measure changes in viscosity and/or density of a test fluid, which is introduced into a

test chamber. There is no disclosure of etched microdroplet transport channels with one or more hydrophobic regions.

- U.S. Patent 5,474,796 to Brennan discloses an apparatus and methods to carry out a large number of chemical reactions on a support surface. Arrays of hydrophilic binding sites are created on a hydrophobic surface. Unlike the present invention, microdroplets are not transported through channels, having one or more hydrophobic regions, etched on the device.
- U.S. Patent 5,416,000 to Allen *et al.* discloses a device and methods for analyte immunoassays. A fluid sample can be received and transported to a measurement region. Unlike the present invention, fluid flow is through flow path elements made of bibulous materials. There is no discussion of etched microdroplet transport channels having one or more hydrophobic regions.
- U.S. Patent 5,304,487 to Wilding *et al.* discloses a microfabricated silicon analytical device (chip) for the analysis of fluid cell containing samples. Samples move through the device in mesoscale flow systems. There is no disclosure of microdroplet transport channels with one or more hydrophobic regions.
- U.S. Patent 5,275,787 to Yuguchi *et al.* discloses an apparatus for separating individual particles in liquid droplets from a suspension of particles in the fluid. Thermal energy is used to generate a bubble and discharge the particle. There is no discussion of an etched microdroplet transport channel with one or more hydrophobic regions.
- U.S. Patent 5,252,743 to Barrett *et al.* discloses a chip upon which particular anti-ligands can be arrayed in particular patterns. The attachment of the anti-ligands relies on caged binding members, which can be spatially activated by irradiation. Ligands can then be screened by applying solutions to the substrate with immobilized anti-ligands. There is no discussion of etched microdroplet transport channels with one or more hydrophobic regions.
- U.S. Patent 5,223,226 to Wittmer *et al.* discloses an electrically insulated needle that can be used to generate an electrospray of droplets from a liquid by

applying an electrical field.There is no discussion of an etched microdroplet transport channel having one or more hydrophobic regions.

- U.S. Patent 4,599,315 to Terasaki *et al.* describes a microdroplet test apparatus that can be used in HLA typing. Following syringe application of samples to the test wells, the test results are viewed through an optical window, and the test solution can be drawn into a tube by capillary action to allow more fluid to be viewed through the optical window. There is no discussion of etched microdroplet transport channels with one or more hydrophobic regions.
- U.S. Patent 4,963,498 to Hillman *et al.* discloses a capillary flow device with internal chambers and capillary channels, through which samples can move by capillary flow and be subjected to various assays. The patent teaches the modification of hydrophobic capillaries to render them hydrophilic. There is no disclosure of etched channels designed for the transport of microdroplets, such channels having hydrophobic regions.
- U.S. Patent 5,192,507 to Taylor *et al.* discloses a biosensor device which uses a biological receptor immobilized on a transducer chip in a polymeric film. Binding of a biomolecule in an applied sample to the receptor can be measured by the transducer.There is no discussion of etched microdroplet transport channels with one or more hydrophobic regions.
- U.S. Patent 4,919,892 to Plumb *et al.* describes an apparatus to detect oil and other lighter-than-water contaminants in an effluent stream, and the means to measure the pH of the effluent stream. The passage of the sample through the apparatus is directed by baffles. There is no discussion of etched microdroplet transport channels having one or more hydrophobic regions.
- U.S. Patent 4,439,526 to Columbus describes a device and method to improve the access of a liquid to an interior transport passage of a capillary transport device. The liquid enters the device from the exterior surface through a cluster of apertures. There is no discussion of etched microdroplet transport channels having one or more hydrophobic regions.
- Chiu *et al.* "Injection of Ultrasmall Samples and Single Molecules into Tapered Capillaries" *Anal. Chem.* 69:1801-1807 (1997) describe a method to prepare

ultrafine tapered capillary tips, with inside diameters in the nanometer range. They show injection of organelle-sized vesicles or single DNA molecules into the tip using suction. There is no discussion of microdroplet transport channels having one or more hydrophobic regions.

- U.S. Patent 5,587,128 to Wilding *et al.* discloses a mesoscale polynucleotide amplification device. The device includes channels and a reaction chamber, microfabricated on a chip. The flow channels may be coated with a reagent to prevent interference with the amplification reaction. There is no discussion of a device with microdroplet transport channels having one or more hydrophobic regions.[1]
- U.S. Patent 5,533,412 to Jerman *et al.* discloses a fluid flow meter which measures flow rate of a fluid by measuring the transit time of a thermal pulse between two separated sensors in the flow channel. There is no disclosure of a device with microdroplet transport channels having hydrophobic regions.[2]
- U.S. Patent 5,585,069 to Zanzucchi *et al.* describes a microscale testing device designed to process many samples in parallel, to reduce the time required for these processes. Samples are moved between wells through channels. There is no discussion of microdroplet transport channels having one or more hydrophobic regions.[3]
- U.S. Patent 5,651,839 to Rauf describes a process to produce polycrystalline films with interconnected grains in a selected direction, which are separated by grain boundaries formed as chains along lines of equal temperature. There is no

---

[1] The hard copy version of this patent, attched to Form PTO-1449, is from the PTO website database. If the examiner request a complete version we will obtain a copy.

[2] The hard copy version of this patent, attched to Form PTO-1449, is from the PTO website database. If the examiner request a complete version we will obtain a copy.

[3] The hard copy version of this patent, attched to Form PTO-1449, is from the PTO website database. If the examiner request a complete version we will obtain a copy.

discussion of a device with microdroplet channels having one or more hydrophobic regions.[4]

- U.S. Patent 5,498,392 to Wilding *et al.* describes a microfabricated, mesoscale PCR device. Samples are processed through a mesoscale flow system, such that the volumes of sample and reagent used are very small. There is no discussion of microdroplet transport channels with one or more hydrophobic regions.[5]
- U.S. Patent 5,048,554 to Kremer describes a gas cylinder valve with a fusible plug constrained by an O-ring. The plug melts at high temperature, thereby freeing a burstable diaphragm to burst if the internal cylinder pressure is sufficient to cause the elastic O-ring to yield. There is no discussion of a device with etched microdroplet transport channels having one or more hydrophobic regions.
- U.S. Patent 4,522,786 to Ebersole describes a multilayered test device in which functional layers are separated by barrier layers. The barrier layers are impregnated with a meltable substance, such that at temperatures below the melting temperature the barrier is intact, but at temperatures above the melting temperature, liquid sample can flow between functional layers. There is no discussion of microdroplet transport channels having one or more hydrophobic regions.
- U.S. Patent 4,457,329 to Werley *et al.* describes a safety pressure regulator. The pressure regulator has an automatic shut-off, which is activated at a predetermined temperature due to melting of fusible material incorporated into the safety device. There is no discussion of etched microdroplet transport channels having one or more hydrophobic regions.
- U.S. Patent 5,364,591 to Green *et al.* describes a contained device for carrying out PCR or immunoassays, in which solids (e.g. beads) are transferred between chambers. The passage of the solids between chambers is controlled by barriers

---

[4] The hard copy version of this patent, attched to Form PTO-1449, is from the PTO website database. If the exaimner request a complete version we will obtain a copy.

[5] The hard copy version of this patent, attched to Form PTO-1449, is from the PTO website database. If the exaimner request a complete version we will obtain a copy.

which can be breached by piercing or liquification upon exposure to heat or centrifugal force. There is no discussion of etched microdroplet transport channels having one or more hydrophobic regions.

- U.S. Patent 5,160,945 to Drake discloses a pagewidth thermal inkjet printhead. Ink is supplied to the individual nozzles through a passage in the structural bar supporting the individual printhead subunits. There is no discussion of a device with etched microdroplet transport channels having one or more hydrophobic regions.
- U.S. Patent 5,700,637 to Southern describes a method to carry out polynucleotide sequence analysis using hybridization to an array of oligonucleotides on a solid surface. There is no discussion of etched microdroplet transport channels having one or more hydrophobic regions.

This Information Disclosure Statement under 37 C.F.R. §§ 1.56 and 1.97 is not to be construed as a representation that a search has been made, that additional information material to the examination of this application does not exist, or that any one or more of these citations constitutes prior art.

Dated: October 5, 2000

Peter G. Carroll
Registration No. 32,837

MEDLEN & CARROLL, LLP
220 Montgomery Street, Suite 2200
San Francisco, California 94104
617/252-3353